REMARKS

Entry of the above amendments and consideration of the following remarks are respectfully requested. Upon entry of the above amendments, this application will contain claims 1-18, and 20-24 pending and under consideration. In the Office Action dated September 25, 2001, Claim 1 was allowed. Objections were raised to claims 3-6, 9-14, 16 and 18 for being dependent upon a rejected base claim but would be allowed if rewritten in independent form. Objections were raised to claim 19 under 37 C.F.R. §1.75 as being substantially a duplicate of claim 1. Claims 2, 7-8, 15, 17 and 20 were rejected under 35 U.S.C. §112. As more fully discussed below, Applicants believe that the claimed invention is patentably and respectfully request reconsideration leading to withdraw of all outstanding rejections and allowance of this application in a timely fashion.

Claim 2 was rejected under 35 U.S.C. §112 as being indefinite for reciting "in situ" generation of single stranded nucleic acids. Firstly, Applicants have amended claim 2 by replacing the term "doubled stranded nucleic acid" with the term --first and second complementary sequences-- to provide antecedent basis with the corresponding term in claim 1. Now considering the claim rejection, it should be noted that it is not the single stranded nucleic acids that are generated in situ, but it is the first and second complementary sequences that are generated from the single stranded nucleic acid. It is respectfully urged that the claimed method as amended is not unclear. The first and second complementary sequences can be generated from a single stranded molecule from methods well know in the art. (See Application, page 4, line 20 through page 5, line 3 and page 9, lines 17-19.)

Claim 7, 8, 17 and 20 were rejected under 35 U.S.C. §112, second paragraph, as indefinite for reciting "at least a portion". Applicants have amended claims 7 and 8 by deleting the term "at least a portion" from the claims. It is believed that claims 7 and 8 as amended are patentable, and withdrawal of the rejections over these claims is requested.

Similarly, Applicants have amended claims 17 and 20 by canceling the term "at least a portion" from the claims. The claimed method can incorporate some modified nucleosides as discussed in the application at page 7, lines 6-10. The modified nucleatide may be, for example, a thiolated or boronated nucleotide or a ribonucleotide. (Application at page 6, lines 10-11.) It should be noted that not all of a particular nucleotide type used in the claimed method need be modified. Nor does the claimed invention require that a specific type of nucleotide, i.e., dATP,

dGTP, dTTP, or dCTP etc., be modified. For example the claimed invention can include a mixture of modified and unmodified dATP nucleotides. Other nucleotides present in the same reaction, i.e., dGTP, dTTP, or dCTP can be modified, but they are not required to be modified. It is believed that claims 17 and 20 as amended are patentable, and withdrawal of the rejections is requested.

Claim 15 was rejected under 35 U.S.C. §112, second paragraph, as indefinite for reciting "a partial degree of resistance to digestion". Applicants have amended claim 15 by deleting the phrase "a partial degree of resistance to digestion" and adding that first, second third and fourth primers --are resistant to digestion by an enzyme functioning as a single stranded active exonuclease--. Support for this amendment can be found in the application, *inter alia*, at page 4, lines 16-19 and page 12, lines 12-18. It is believed claim 15 as amended is patentable. Consequently, withdrawal of the rejection is requested.

Claim 19 was rejected for being a substantial duplicate of claim 1. Claim 19 has been canceled. Accordingly this rejection is moot.

Objections were raised to claims 3-6, 9-14, 16 and 18 for being dependent upon a rejected base claim. These claims depend either directly or indirectly from claim 1. Claims 3, 5, 9-14, 16, and 18 were amended in a preliminary amendment to depend from claim 1. Claim 4 depends from claim 3, and claim 6 depends from claim 5. Claim 1 has been allowed. Since the base claim has been allowed, claims 3-6, 9-14, 16 and 18 are allowable.

New claims 21-24 have been added. Support for claims 21 and 22 can be found in the application, *inter alia*, at page 4, line 20 through page 5, line 3; page 9, lines 17-19; and in Figs 3 and 4. Support for claims 23 and 24 can be found in the application at page 12 lines 4-18 and original claims 14 and 15.

Applicants respectfully that the pending claims are patentable. Accordingly, reconsideration leading to withdraw of all the rejections under 35 U.S.C. § 112 and allowance of this application containing claims 1-18 and 20-24 are respectfully requested. Additionally, the

Examiner is invited to telephone the undersigned attorney if there are any questions about this submission or other formal matters, which may be addressed in that fashion.

Respectfully submitted,

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VERSION WITH MARKING TO SHOW CHANGES MADE

2. (Twice Amended) A method as claim 1 wherein the complementary first and second nucleic acid sequences are ~~double stranded nucleic acid molecule is~~ generated *in situ* from a single stranded nucleic acid molecule.

7. (Twice Amended) A method as claimed in claim 1 wherein the third primer is of a sequence corresponding to ~~at least a portion of~~ the sequence in the first primer on the 5' side of the digestion resistant region of that primer.

8. (Twice Amended) A method as claimed in claim 1 wherein the fourth primer is of a sequence corresponding to ~~at least a portion of~~ the sequence in the second primer on the 5' side of the digestion resistant region of that primer.

15. (Twice Amended) A method as claimed in claim 1 wherein the 5'-ends of the first, second, third and fourth primers ~~have a partial degree of resistance to digestion~~ are resistant to digestion by an exonuclease functioning as a single strand active exonuclease.

17. (Twice Amended) A method as claimed in claim 1 wherein ~~at least a portion of~~ at least one of the nucleoside triphosphates provided as (e) of claim 1 is~~/are a~~ modified such that when it is incorporated in a growing nucleic acid chain it is resistant to digestion by the exonuclease.

20. (Twice Amended) A method of amplifying complementary first and second nucleic acid sequences each of which has a binding region at its 3' end, the method comprising treating the separated single stranded sequences with

(a) first and second primers each capable of hybridising to the 3'-binding regions of the first and second strands respectively and each including remote from its 5'-end a digestion resistant region which, with the primer hybridised to a complementary 3'-binding region, allows only partial digestion of the primer by the enzyme (d) having 5'-double strand specific exonuclease activity,

(b) third and fourth primers each having a degree of sequence homology with the particularly digestible regions of the first and second primers respectively whereby the third and fourth primers are capable of hybridising to the 3'-binding regions of the first and second strands respectively,

(c) an enzyme having strand displacing polymerase activity,

(d) an enzyme having 5' double stranded specific exonuclease activity, said enzyme (d) possibly being provided by enzyme (c) in the case where the latter also has the required exonuclease activity, and

(e) nucleoside triphosphates~~, at least a portion of at least one of~~ which ~~is~~ are modified such that when ~~it is~~ incorporated into a growing nucleic ~~it is~~ they are resistant to digestion by the exonuclease~~.~~

~~———————~~under conditions permitting hybridisation, exonuclease digestion and strand displacement polymerisation thereby producing an amplified amount of the first and second strands.

Claim 19 has been canceled.

Claims 21-24 have been added.

21. (New) The method of claim 1 wherein the third primer is capable of hybridizing to the 3'-binding region for the first primer which is complementary to the 5'-side of the digestion resistant region of the first primer.

22. (New) The method of claim 1 wherein the fourth primer is capable of hybridizing to the 3'-binding region for the second primer which is complementary to the 5'-side of the digestion resistant region of the second primer.

23. (New) A method as claimed in claim 1 wherein the 5'-ends of the first, second, third and fourth nonhybridized primers are resistant to digestion by 5'-double strand specific exonuclease.

24. (New) A method as claimed in claim 1 wherein the 5'-ends of the first, second, third and fourth primers incorporate modified nucleotides which are resistant to digestion by 5'-double strand specific exonuclease.